

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Methods

We identified patients fulfilling the following criteria:

- COVID-19 vaccination (ChAdOx1 nCoV-19 or Ad26.COV2.S) four to 30 days previously,
- Severe headache as leading symptom
- Thrombocytopenia and high D-dimer at admission.
- Absence of CVST on initial imaging (computed tomography, angiography, magnetic resonance, angiography or digital subtraction angiography)
- positive anti-PF4/heparin IgG ELISA

For all patients, headache-related information (time of onset; type), laboratory findings on admission (platelet count; D-dimer), concomitant neurological deficits, extracranial thrombosis, therapy-related data (start, type) and neuroimaging data (method, latency, results) were analyzed. In all patients, laboratory workup of anti-PF4 antibodies by anti-PF4/heparin IgG ELISA and for heparin- and PF4-dependent platelet activating antibodies was performed (2).

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Legend Supplementary Table 1

Supplementary Table 1 summarizes demographic data, initial symptoms (type, onset, analgetics), time of admission, initial laboratory findings (platelet count, D-dimer, fibrinogen), anti-PF4/heparin IgG ELISA results, extracranial thrombosis (location, time of detection), VITT treatment (type, time of application), neuroimaging (type, time of imaging), cerebrovascular complications (intracranial hemorrhage [ICH] and/or CVST) and neurological outcome (modified Rankin scale).

Patient gender, age	Initial symptoms, onset (days after vaccination), headache intensity (1-10), Analgetics	Time of initial admission (days after onset of headache) & laboratory findings	Anti-PF4/heparin IgG-ELISA / PF4-dependent platelet activating antibodies	Extracranial thrombosis, days after vaccination	Start of treatment, days after onset of headache	Neuroimaging, days after onset of headache	Cerebrovascular Complication	Neurological Outcome (modified Rankin Scale)
Patient 1 f, 48y	Right hemicranial headache, 5d Headache intensity 6/10 metamizole, paracetamol, piritramide	2d Platelets 102,000/ μ L D-Dimer 34mg/L*) Fibrinogen 1.75g/L*)	Strongly positive/ OD 3.40 PF4-dependent platelet activating antibodies +++	Pulmonary embolism, 13d	IVIG, 5d dexamethasone, 5d argatroban, 6d	CT, 2d CT, 5d DSA, 5d	- ICH	Slight disability (modified Rankin Scale 2)
Patient 2 m, 63y	Holocephalic headache, 18d Headache intensity 10/10 metamizole, piritramide	3d Platelets 26,000/ μ L D-dimer 36mg/L Fibrinogen 4.49g/L	Strongly positive/ OD 3.47 PF4-dependent platelet activating antibodies +++	Pulmonary embolism, splanchnic veins, 14d	IVIG, 8d argatroban, 9d	CT, 3d CT, 5d CT, 8d	- - ICH, CVST	Dead (modified Rankin Scale 6)
Patient 3 m, 47y	Holocephalic headache, transient cognitive impairment, 6d Headache intensity 6/10	0d Platelets 116,000/nL D-dimer 28mg/L	Strongly positive/ OD 2.74 PF4-dependent platelet activating	Deep arm venous thrombosis, 14d	IVIG, 2d dexamethasone, 7d argatroban, 7d	MRI, 0d CT, 3d CT, 4d DSA, 4d	- CVST ICH, CVST CVST	Moderate disability (modified Rankin Scale 3)

	metamizole, paracetamol, ibuprofen, piritramide, oxycodone	Fibrinogen 3.74g/L	antibodies +++					
Patient 4 f, 24y	Holocephalic headache, hematoma, shoulder & abdominal pain, 14d Headache intensity n.a. ibuprofen, metamizole, diclofenac	7d Platelets 93,000/ μ L D-dimer 32mg/L Fibrinogen n.a.	Strongly positive/ OD 3.23 PF4- dependent platelet activating antibodies +++	Pulmonary embolism, 21d	apixaban, 7d	CT, 7d MRI, 8d	- -	No symptoms (modified Rankin Scale 0)
Patient 5 f, 32y	Holocephalic headache, 9d Headache intensity 7/10 ibuprofen, metamizole	2d Platelets 65,000/ μ L D-dimer 14mg/L Fibrinogen 2.61g/L	Strongly positive§ PF4- dependent platelet activating antibodies not tested	-	IVIG, 3d dexamethasone, 3d apixaban, 3d	CT, 2d MRI, 3d	- -	No symptoms (modified Rankin Scale 0)
Patient 6 f, 23y	Holocephalic headache, 11d Headache intensity 8/10	0d Platelets 112,000/ μ L D-dimer	Strongly positive/ OD 3.18 PF4- dependent	-	IVIG, 1d argatroban, 1d	MRI, 0d MRI, 3d	- -	No symptoms (modified Rankin Scale 0)

	paracetamol, ibuprofen	29mg/L Fibrinogen 1.99g/L	platelet activating antibodies neg. pretreatment with IVIG					
Patient 7 f, 31y	Holocephalic headache with thunderclap onset, 6d Headache intensity 7/10 metamizole	0d Platelets 42,000/ μ L D-dimer 10mg/L Fibrinogen 2.56g/L	Strongly positive/ OD 3.60 PF4- dependent platelet activating antibodies +++	-	IVIG, 1d apixaban, 1d	MRI, 1d MRI, 8d	- -	No symptoms (modified Rankin Scale 0)
Patient 8 f, 55y	Right hemicranial and retrobulbar headache, 8d Headache intensity 8/10 metamizole	5d Platelets 71,000/ μ L D-dimer 6.1mg/L Fibrinogen 4.26g/L	Strongly positive/ OD 3.16 PF4- dependent platelet activating antibodies +++	-	phenprocoumon ongoing**)	CT, 5d	-	Fatigue (modified Rankin Scale 0)
Patient 9 f, 74	Headache (other), 7d Headache intensity 8/10 paracetamol	2d Platelets 17,000/ μ L D-dimer 35mg/L Fibrinogen 0.74g/L	Strongly positive/ OD 1.93 PF4- dependent platelet activating antibodies +++	-	IVIG, 4d argatroban, 7d	MRI, 3d CT, 12d	- -	No symptoms (modified Rankin Scale 0)

Patient 10 f, 54	Holocephalic headache, 8d Headache intensity 5/10 ibuprofen	3d Platelets 66,000/ μ L D-dimer 4.3mg/L Fibrinogen 3.07g/L	Strongly positive/ OD 3.42 PF4-dependent platelet activating antibodies +++	-	apixaban, 9d ^{***)}	CT, 3d	-	Fatigue (modified Rankin Scale 0)
Patient 11 f, 51	Headache (other), 9d Headache intensity 4/10 non-steroidal anti-inflammatory drugs, not further classified	5d Platelets 97,000/ μ L D-dimer 1.7mg/L Fibrinogen n.a.	Strongly positive/ OD 3.16 PF4-dependent platelet activating antibodies +++	-	rivaroxaban, 5d	CT, 5d MRI, 5d	- -	No symptoms (modified Rankin Scale 0)

Y = years; f = female, m = male; d = day; OD = optical density; CT = computed tomography; MRI = magnetic resonance imaging; IVIG = high dose intravenous immunoglobulins; DSA = differential substrating angiography

*¹) D-dimer and fibrinogen level from second admission (was not tested on first admission)

**²) Patient was already under phenprocoumon anticoagulation due to atrial fibrillation

***³) Apixaban was stopped after one day due to drug exanthema

§ tested by another laboratory only qualitative data available